Version with Markings to Show Changes Made

Claim 8 has been amended as follows.

8. (Amended) A method according to claim 6 wherein said scoring function is selected from the group consisting of a [Van] van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic salvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

Claim 18 has been cancelled.

Appendix of Pending Claims

1. A method for modulating the immunogenicity of a target protein, said method comprising:

a) inputting a protein backbone structure with variable residue positions of a target protein into a computer;

b) computationally generating a set of primary variant amino acid sequences; and,

c) applying a computational immunogenicity filter against said set to identify at least one candidate variant protein.

2. A method according to claim 1 further comprising testing said candidate variant protein to determine if said immunogenicity is altered relative to said target protein.

3. A method according to claim 1 further comprising classifying each variable residue position as either a core, surface or boundary residue.

4. A method according to claim 1 wherein said computationally generating step comprises a DEE computation.

5. A method according to claim 4 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

6. A method according to claim 1 wherein said set of primary variant amino acid sequences are optimized for at least one scoring function.

7. A method according to claim 6 wherein said set of primary variant amino sequences optimized for at least one scoring function comprises the globally optimal protein sequence.

8. (Amended) A method according to claim 6 wherein said scoring function is selected from the group consisting of a van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic salvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

9. A method according to claim 1 wherein said computationally generating step includes the use of a Monte Carlo search.

10. A method according to claim 1 wherein said target protein is from a non human species and said candidate variant protein exhibits reduced immunogenicity in humans.

11. A method according to claim 1 wherein the immunogenicity of said candidate variant protein is reduced relative to said target protein.

12. A method according to claim 1 wherein said candidate variant protein is non-immunogenic.

13. A method according to claim 11 or 12 wherein said candidate variant protein is more stable than said target protein.

14. A method according to claim 1 wherein said modulating the immunogenicity of said target protein comprises modifying the amino acid sequence that binds to an MHC molecule.

15. A method according to claim 14 wherein said MHC molecule belongs to MHC class I.

16. A method according to claim 14 wherein said MHC molecule belongs to MHC class II.

17. A method according to claim 1 wherein said modulating the immunogenicity of said target protein comprises modifying an amino acid sequence encoding a T cell epitope.

19. A method according to claim 1, further comprising computationally analyzing said variant protein for maintenance of native fold and stability.